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Dr. Joshua Lederberg
Stanford University
Palo Alto, California

Dear Dr. Lederberg:

I am grateful for your comments and for the reference to Munson and Bridges.

I agree with you that the only interest in the work is the conclusion that the increase in the mutants is due to an increase in mutation rate and not merely to selective growth. It was for this reason that I carried out the long series of determinations of the mutation rates by your elegant null fraction method. In my opinion this is the only valid method. These experiments showed about the same increase in the mutation rate of the log culture compared to the control as do the kinetic experiments.

The assumption that the increase in the mutants is due to an increase in their growth rate, so that $B > A$, accounts for the initial increase in the mutants, but cannot account for the equilibrium ratio.

The ratio of mutants/wild in a culture in continuous log growth with negligible mutation rate is

$$\ln M/W = (B-A)t + \ln M_0/W_0$$

If $B = A$, no change occurs
$B > A$, $M/W \to \infty$
$B < A$, $M/W \to 0$

In order to have an equilibrium, it is necessary for the mutation rate to exactly compensate for the difference in growth rate so that $M/W_{\text{equilibrium}} = \frac{c}{A-B}$.

With best regards

John H. Northrop

Northrop, J. H

NCM 3/12/65

P. S. Please send me a reprint of your paper in J. Mol. Biol. 9, 683, 1964